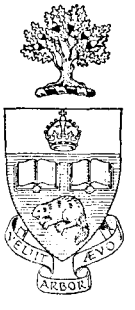
UNIVERSITY OF TORONTO

DOUBLE FORTIFICATION OF SALT

Phase 1 Final Report



DEPARTMENT OF CHEMICAL ENGINEERING
AND APPLIED CHEMISTRY

DOUBLE FORTIFICATION OF SALT

Phase 1 Final Report

Prepared for
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Executive Summary

Over the past decade the magnitude and consequences of global malnutrition have been increasingly recognized. Deficiencies in small quantities of micronutrients, especially iodine and iron, severely affect more than a third of the world's population. In the less developed countries these deficiencies have serious public health consequences, especially for women and young children.

Salt is an ideal carrier of micronutrients. Iodized or iodated salt has long been available in developed countries and the problem of iodine deficiency has been virtually eliminated in North America and most European countries. The double fortification of salt with both iodine and iron is an attractive approach to the reduction of both anemia and IDD. Unfortunately when iron and iodine are both added to salt the iodine is converted to elemental; iodine, which can sublime, and thus it is rapidly lost. Iron is also readily oxidized to the ferric form, which has a lowered bioavailability. Despite the apparent chemical incompatibility of iron and iodine, two previously published reports indicated that it may be possible to stabilize iodine on salt in the presence of iron. Based on the work of Mannar et al. we initiated the present research program to investigate the effect of packaging materials and environmental conditions on the stability of iron and iodine double-fortified salt. In this study we have also examined the technological problems associated with the field application of salt double-fortification.

Samples of salt were fortified to contain 50 mg/kg iodine and 1,000 mg/kg iron using potassium iodide and ferrous fumarate respectively. Four techniques were used, in which: 1. - all ingredients were blended as powders; 2. - KI was sprayed on the salt as a solution, while the iron was added as a powder; 3. - this treatment was repeated with the further addition of 1% $MgCl_2$, a naturally occurring hygroscopic contaminant of crude sea salt; and 4. - KI was coprecipitated with CaCO3 and this solid was blended with salt and ferrous fumarate as powder

Four packaging materials were tested: high-density polyethylene bags, paper bags, polypropylene jars and low-density polyethylene bags. The samples were stored under room temperature and humidity, elevated temperature and humidity or elevated temperature and low humidity to reproduce the typical storage conditions expected in most developing countries.

The samples were analyzed after 1, 2, 3 and 6 months. The results clearly indicated that iodine is rapidly lost after initial mixing, but the amount retained remains essentially constant after the first 1-2 months. In most treatments approximately a third of the iodine initially applied to the sample were retained.

Calcium chloride did not have a sparing effect on iodine, despite contrary indications in the literature.

The iron content, of course remained constant. More important was the fact that the HCl soluble iron, which is representative of the amount of bioavailable iron, remained essentially unchanged by any of the treatments.

We found that application of the iodine compounds as a solution resulted in a more even distribution of the iodine throughout the sample. Ferrous fumarate could not be applied as a solution, due to its low water solubility, and the iron rapidly segregated during normal handling of the sample containers, resulting in Fe concentrations that ranged between 25% and 175% of the initial 1000 ppm in different parts of the storage container.

Due to its low solubility, relatively dark colour, and tendency to turn to a darker colour with time, in our opinion ferrous fumarate is not the preferred carrier for iron in salt.

The effect of the packaging materials was overshadowed by the other variables. None of the packaging materials was clearly better than any other. This may have been due to the fact that the polymer bags were not heat sealed, and thus some moisture penetration was possible.

The highest iodine losses were observed at 40° C, 100% relative humidity. This is expected, especially in light of the comments above. We were hoping that the waterproof barrier materials would protect the salt, but this will not happen in an unsealed bag, and accordingly, it is unlikely to happen in the end-users' homes.

The most important finding of the study was the effect of magnesium chloride, a hygroscopic impurity often found in unpurified salt. It dramatically increased the moisture content of the salt, and resulted in the almost immediate loss of more than 90% of the added iodine.

The work demonstrated that it is important that adsorbed water, iron and iodine do not come into contact on the salt surface. The use of refined (purified) salt is technically feasible, but it would be economically unviable. Better results could be achieved by encapsulating the iodine or perhaps the iron compound in an inert carrier such as sodium hexametaphosphate or dextrin, or to prepare pre-mixes with high concentrations of iron and iodine separately, and use these to prepare the final formulation.

Despite of the losses of iodine experienced in this project, we are confident that a cost-effective, simple industrial process for double fortification is possible, but its development requires the systematic solution of the specific problems identified in this study. If losses of iodine experienced in this study would be in the same ratio at higher addition levels, say 150 mg/kg, then sufficient amount of iodine could be stabilized for six months. This will be tested in the proposed next phase of the program.

Future direction of our work will include:

Evaluation of several promising iron compounds for stability and compatibility with iodide and iodate;

Improved mixing, by two-stage mixing of ingredients to ensure even distribution of iron and iodine;

Preparation of separate pre-mixes of iron and iodine, to simulate *in-situ* addition to local salt source;

Encapsulation of iodine, and perhaps iron in a matrix that prevents their reactions and degradation. The forming of a physical barrier between the iodine compound and iron would stabilize the system. Encapsulating agents could include such stabilizers as sodium hexametaphosphate, dextrin, or even purified salt.

The proposed program of laboratory investigations attached in the appendix will demonstrate the feasibility of several approaches, forming the basis of an effective technological scale-up.

Background

Over the past decade the magnitude and consequences of global malnutrition have been increasingly recognized. Deficiencies in small quantities of micronutrients, especially iodine and iron, severely affect more than a third of the world's population. In the less developed countries these deficiencies have serious public health consequences, especially for women and young children.

The lack of iodine in the soil and water and thus, in food, leads to Iodine Deficiency Disorders (IDD) which includes goiter and a wide spectrum of mental and intellectual defects of varying degrees of severity including cretinism, paralysis and deaf-mutism. IDD can also lead to stunted growth and development, miscarriages, still births and infant deaths.

Anemia due to iron deficiency results in a major reduction in work capacity and impaired immune response which leads to a higher incidence of infection, increased risk of maternal and fetal morbidity, and reduction in body growth. The combined impact of these deficiencies results in a severe retardation of social and economic development of entire populations.

The fortification of commonly used foods is an important component of the strategy to combat micronutrient malnutrition. Salt is an ideal carrier of micronutrients in view of its almost universal coverage and uniform regional consumption. Iodized or iodated salt has long been available in developed countries and the problem of iodine deficiency has been virtually eliminated in North America and most European countries. Yet, because the severity and extent of IDD were not widely recognized until recently most of the affected countries begun to take steps towards universal iodization of salt only in the past few years. Many developing countries which now have iodization programs in place, have begun to achieve a significant reduction in IDD.

Encouraged by the progress made in several countries in implementing successful salt iodization programs, efforts have been directed to examining the feasibility of fortifying salt with iron along with iodine. With production and monitoring infrastructure for iodization programs already in place, such an integration and coordination would be the most cost efficient method of ensuring adequate levels of both iron and iodine in the population.

This poses a challenge in developing a formulation in which both the iodine and iron are stable and bioavailable. When attempts were initially made in the mid 1980's to incorporate iodine and iron in salt at the same time, there were problems with the stability of both micronutrients.

Salt can be iodized with either potassium iodide (KI) or iodate (KIO_3). While the former is stable in refined dry salt, the latter shows better stability in low-quality salt in poor packaging. Ferrous iron is stable in an acid medium, whereas the iodine salts are slightly alkaline in solution. In an alkaline medium

ferrous iron can oxidize to ferric, which is not as soluble, and therefore the bioavailability of iron is lowered.

When the iron is added as ferrous sulphate to an impure salt, which is hygroscopic, the system becomes acidic. In an acid medium the oxidation of the iodide to iodine takes place rapidly, producing free iodine, which vaporizes, and is lost. Potassium iodate is an oxidizing agent. When it is mixed with ferrous iron it tends to oxidize Fe^{++} to Fe^{+++}, while it is reduced to the volatile I_2 or KI. In order to tackle the problem of incompatibility between iron and iodine salts, two approaches have been proposed: using ferrous sulphate with a chelating polyphosphate stabilizer along with potassium iodide (Rao, N.B.S. 1990); and using ferrous fumarate along with potassium iodide (Venkatesh Mannar et al. 1989). In India both approaches have been tested and workable formulations have been proposed:

i. Narasinga Rao of the National Institute of Nutrition developed a formula using ferrous sulphate (1000 ppm Fe), potassium iodide (20 ppm I_2) and a stabilizer (a chelating polyphosphate). He has reported that the bioavailability and stability of the double fortified salt under different conditions of storage and acceptability were found to be good. The formulation proposed by Rao is:

Ferrous sulphate ($FeSO_4.7H_2O$)	5000 ppm	(1000 ppm Fe)
Potassium iodide	40 ppm	(30 ppm I_2)
Stabilizer (phosphate)	1 %	

However; the analysis of salt from a larger-scale test showed less than 3% of the initial iodine levels after distribution.

ii. After tests with various iron and iodine compounds, Venkatesh Mannar et al. (1989) reported that ferrous fumarate and potassium iodide represent a workable combination without stabilizers. Ferrous fumarate, which is a poorly soluble, but biologically well absorbed iron compound, has a pH close to 7 in solution, and it should be stable to oxidation. While it is naturally reddish brown in colour, at the small concentration of 3 g/kg salt (~1000 ppm Fe) it imparts only a light pink-brown colour to the salt, and did not seem to deteriorate with time. At this concentration it is less likely than $FeSO_4.7H_2O$ to cause organoleptic problems. Owing to the fine particle size of ferrous fumarate in its usual commercial form (200 mesh), it can be added in a dry form as a rich premix and still get it evenly dispersed in the salt. Its toxicity is less than that of ferrous sulphate, and its effect on the stomach lining is less irritating than that of ferrous sulphate or ferrous gluconate. Potassium iodide, unlike potassium iodate is not an oxidizing agent, and therefore it will not react with ferrous fumarate. Salt fortified with ferrous fumarate and potassium iodide is of a very light brownish colour and does not deteriorate with time, provided that it is kept sealed in waterproof packing. They proposed the following formulation for double fortification of salt:

Ferrous fumarate	3050 ppm	(1000 ppm Fe)
Potassium iodide	65 ppm	(50 ppm I_2)

The test report indicated that iron and iodine levels in the double-fortified salt were not depleted in 8 weeks of storage after preparation.

Due to the great potential of double fortification for the reduction of serious deficiency diseases in developing countries, we proposed to investigate the effect of storage conditions, storage materials and applications technology on the stability and availability of iron and iodine in double fortified salt prepared by the method proposed by Mannar et al. in 1989, using KI and ferrous fumarate. Ferrous fumarate is the form of iron most often used in multi-vitamin and mineral formulations. Although it is more expensive than $FeSO_4$ it is stable in the presence of KI and has an acceptable colour and flavour as well as high bioavailability.

The proposal originally submitted in 1991 was accepted by the Micronutrient Initiative in 1993.

The results of the tests indicated that there are many technological problems and opportunities with double fortification of salt, and it would not be productive to extend the current storage stability tests beyond the six month mark. Accordingly, it was agreed that an extensive review of fortification techniques will be performed as Phase 2 of this program under a separate program. The proposed scope of Phase 2 is attached in Appendix 2. The following report summarizes the work performed to date on Phase 1.

Objectives

The objective of the research program was to test the stability of double fortification of salt using ferrous fumarate and potassium iodide reported by Venkatesh Mannar et al. (1989), under a variety of storage conditions.

Experimental Techniques

Materials

The following materials were used:

-ferrous sulphate (MW = 278.01), laboratory grade, potassium iodide (MW = 166), hydrochloric acid (MW = 36.46), potassium iodate (MW = 214), potassium thiocyanate (MW = 97.18) magnesium chloride hexahydrate (MW = 203.30), calcium carbonate (MW = 100.09), analytical grade - BDH, Toronto;

- iron atomic adsorption standard - SCP Science, Toronto,
- sodium hexametaphosphate (MW = 611.77), reagent grade and nitric acid (69.0-71.0%), analytical grade - J.T. Baker, Toronto

salt:, food grade - non iodized, Toronto Salt Chemical, Toronto

Sample treatment

Three kg samples of salt were fortified to contain 50 mg/kg iodine and 1,000 mg/kg iron using potassium iodide and ferrous fumarate respectively. The mixtures were blended to ensure uniformity using either a 7L double-cone blender (Patterson Industries Ltd., Toronto) or a 5L ribbon blender (LeRoy Somer - LSTronics).

Four treatment techniques were used as indicated in the following. Each treatment was performed in duplicate.

A. **Powder addition** - Potassium iodide and ferrous fumarate were added to the salt as a powder, and blended for 15 min. in a double-cone blender. In later samples a ribbon blender was used.

B. **Aqueous solution of KI** (about 5% w/v) was added to salt and mixed for 15 minutes. Then the salt was dried at 110 °C for about 10 minutes. Ferrous fumarate powder was then added to the mixture and blended again for another 15 minutes. (In the original proposal, aqueous solution of KI and ferrous fumarate were to be used. However, since ferrous fumarate is almost insoluble, we used an aqueous solution of KI and ferrous fumarate in powder form.)

C. **KI coprecipitate with $CaCO_3$.** - Iodine was added as a powder prepared by co-drying a solution containing 4 g $CaCO_3$ per g KI. This solid was blended with salt and ferrous fumarate as powder for 15 minutes. According to the original proposal, either ferrous fumarate or ferrous sulphate were to be added. We chose ferrous fumarate.

D. **Hygroscopic Sample -** One additional series of samples were prepared by the addition of 1% $MgCl_2$ (a naturally occurring hygroscopic contaminant) to the salt. in an effort to determine the effect of this contaminant on the stability of double-fortified salt. First, salt was mixed with an aqueous solution of KI (5% w/v) for 10 minutes and dried at 110°C for about 10 minutes. Then, ferrous fumarate powder was added and mixed for another 10 minutes. Finally, $MgCl_2$ was added and mixed again for 10 minutes. Samples prepared by this treatment were packaged only in low-density polyethylene bags. (In the original proposal, aqueous solution of KI and ferrous fumarate were to be used. However, since ferrous fumarate is almost insoluble, we used an aqueous solution of KI and ferrous fumarate in powder form.)

Packaging materials

Samples of preparations of A, B, and C above were packaged in 500 g portions as follows:

1. High-density polyethylene bags

2. Paper bags

3. Polypropylene jars (In the original proposal PVC containers were to be used, but these were not available.)

4 Low-density polyethylene bags

Storage conditions

The packages were stored under three conditions:

1. ambient room temperature and humidity (~ 22 °C, 50-70% RH),

2. elevated temperature and humidity (~ 40 °C, 100% RH), and

3. elevated temperature and low humidity (~ 40° C, ~ 60 % RH).

The high temperature and high humidity was maintained by using a controlled temperature oven, in which the air was saturated by exposure to a tray of water. The high temperature/low humidity conditions were maintained in an environmental chamber manufactured by Associated Environmental Systems Division of Craig Systems Corporation.

ANALYTICAL METHODS

Total iron

Total iron is measured by Atomic absorption analysis

1. Approximately 200 mg sample was weighed accurately into a 40 ml volumetric test tube.

2. Using a Brinkman Instruments dispenser 10 mL digestion solution, consisting of concentrated HNO_3 and HCl (1:1 v/v).

3. Samples were digested by boiling off approximately 75% of the liquid on a hot plate.

4. The digested samples were allowed to cool and then the volume of the solution was made up to 40 mL with deionized water.

5. The absorbance at 248.3 nm was recorded, using a Perkin Elmer Model 703 atomic absorption spectrophotometer with an iron hollow cathode lamp as the light source.

This accuracy and precision of the method were verified by using ferrous fumarate standards. The results are presented in Table 1:

Table 1. Reproducibility of iron analysis by atomic absorption

Sample Fe: 5 ppm	1	2	3	4	5	6	7	Avrg	STDV
Fe (ppm)	5.05	4.88	4.98	4.77	4.99	4.89	5.05	**4.94**	**0.10**

In vitro digestible iron, or HCl soluble iron

The solubility of iron in 1N HCl represents the solubility of iron in the human stomach, and therefore it gives a good indication of the digestibility of the iron present in the sample. The following procedure was followed.

1. Approximately 200 mg sample was weighed accurately into a 40 ml volumetric test tube.

2. Each sample was made up to 40 mL using 1.000N HCl solution in a volumetric test tube.

3. Samples were digested by stirring at room temperature.

4. The absorbance at 248.3 nm was recorded, using a Perkin Elmer Model 703 atomic absorption spectrophotometer with an iron hollow cathode lamp as the light source.

Moisture

The moisture content was determined gravimetrically. Samples of salt were weighed, then dried at 180°C for 16 hours and reweighed.

Iodine

Iodine was measured by neutron activation analysis.

1. Approximately 1.25 g of salt is accurately weighed into a polyethylene vial. To decrease the interference due to the presence of large concentration of chlorine in the sample, the sample is shielded with cadmium.

2 It is irradiated at 1 kW power using a neutron flux of 5.0×10^{11} cm^{-2} sec^{-1} for 3 minutes using the University of Toronto's SLOWPOKE nuclear reactor.

3. The samples are removed from the reactor, and rested for 6 minutes.

4. After 6 minutes delay the gamma emission at 443 keV is measured using a hyperpure germanium based gamma ray spectrometer.

5. The iodine content is calculated based on a calibration established by a series of spiked samples that covered the range of 5 to 250 mg iodine per kg salt. The relative standard deviation of the analysis was determined to be 2%.

Colour

The colour of the samples were compared visually. Several representative samples were measured using a Hunter Laboratories L,a,b colour measurement system, using the facilities of Ryerson Polytechnical University.

Taste

One percent solutions of salt in deionized water were prepared and compared in a triangle test.

Results

Moisture

The moisture content of the mixed salt samples were low, as expected. The strong hygroscopic effect of magnesium chloride is evident: samples containing 1% $MgCl_2$ had moisture levels that were 10 to 12 times that of other samples that were free of this hygroscopic impurity. The results are summarized in Table 2.

Table 2. Moisture content for each batch:

	Powder Addition		KI Solution		$CaCO_3$ Addition		$MgCl_2$ Addition	
	Moisture	Avrg	Moisture	Avrg	Moisture	Avrg	Moisture	Avrg
1	0.06%		0.04%		0.06%		0.68%	
	0.05%		0.07%		0.05%		0.73%	
	0.05%		0.06%		0.07%		0.72%	
	0.05%		0.04%		0.06%		0.64%	
	0.06%	0.06%	0.05%	0.05%	0.04%	0.05%	0.68%	0.69%
2	0.07%		0.04%		0.06%			
	0.05%		0.05%		0.05%			
	0.06%		0.06%		0.05%			
	0.10%		0.05%		0.04%			
	0.10%	0.08%	0.05%	0.05%	0.06%	0.05%		

The moisture contents of all the samples are increased by 50% - 150%, in the first two months of the test. (Table 3.) The changes in moisture content show no pattern, perhaps due to the large errors in the measurements since the moisture contents are very low.

Table 3. Moisture contents of the samples after 2 months.

*No	H_2O %	Increase %	No	H_2O %	Increase %	No.	H_2O %	Increase %
A1a	0.127	105	**B1a**	0.084	36	**C1a**	0.135	68
A1b	0.121	96	**B1b**	0.101	63	**C1b**	0.103	29
A1c	0.102	65	**B1c**	0.089	44	**C1c**	0.160	99
A2a	0.177	186	**B2a**	0.091	47	**C2a**	0.104	30
A2b	0.126	103	**B2b**	0.114	84	**C2b**	0.098	23
A2c	0.158	155	**B2c**	0.156	151	**C2c**	0.099	24
A3a	0.116	88	**B3a**	0.134	116	**C3a**	0.102	28
A3b	0.105	69	**B3b**	0.091	46	**C3b**	0.128	60
A3c	0.160	158	**B3c**	0.113	83	**C3c**	0.115	43
A4a	0.147	138	**B4a**	0.097	57	**C4a**	0.158	97
A4b	0.085	38	**B4b**	0.120	94	**C4b**	0.086	7
A4c	0.162	161	**B4c**	0.083	34	**C4c**	0.117	46
D4a	0.982	114	**D4b**	0.806	75	**D4c**	1.299	182

* A, B, C, and C: the treatments of powder addition, KI solution addition, $CaCO_3$ addition, and $MgCl_2$ addition, respectively.

1, 2 , 3, and 4: the package materials of high-density polyethylene bags, paper bags, polypropylene jars, and low density-density polyethylene bags, respectively

a, b, and c: storage conditions of room conditions, 40°C & 100% RH, and 40°C & 60% RH, respectively.

The moisture content did not vary greatly over the rest of the period of testing. The results are presented in Table 4.

Blending and sampling

We were surprised at the great diversity of analytical results we have initially obtained. We determined that the blending procedure itself introduces a great variability in the results. The double-cone blender does not produce a uniform blend with iron even after a long mixing period. Since the mixing generates some heat, this can lead to iodine loss in the presence of moisture and iron. With a dark iron compound we could see variations in colour when the samples were spread out on a flat surface. This variability was reduced, but not eliminated by switching to a ribbon blender.

Table 4. Moisture Change (%)

Treat-ment	Powder addition			KI solution addition			CaCO3 addition			MgCl2 addition		
	0 mnth 2 mo	100 3 mo	6 mo	0 mnth 2 mo	100 3 mo	6 mo	0 mnth 2 mo	100 3 mo	6 mo	0 mnth 2 mo	100 3 mo	6 mo
1A	205	282	271	135	181	167	165	157	170			
1B	195	206	248	163	185	195	126	141	231			
1C	165	184	317	144	150	200	195	187	291			
2A	285	252	189	147	139	198	127	139	127			
2B	203	216	206	184	211	157	120	124	190			
2C	255	252	347	252	229	219	121	148	195			
3A	187	252	183	216	219	270	124	141	148			
3B	169	279	387	147	163	155	156	163	114			
3C	187	239	315	182	185	142	140	139	131			
4A	237	285	357	156	190	209	193	198	237	129	128	128
4B	137	202	284	194	203	165	105	138	170	106	110	105
4C	261	240	302	134	166	185	143	139	130	161	157	154

1: high-density polyethylene bags,2: paper bags, 3: polypropylene jars, 4: low density-density polyethylene bags

A: room conditions, B: 40 °C+100% RH, C: 40°C + 60% RH

Since the samples were not uniform, variations of iodine content from 15 to 120 mg/kg were obtained in samples nominally containing 55 mg/kg I_2. We found that some of the variability was due to the segregation of the added KI and ferrous fumarate powders. Since these had a much smaller particle size than the salt, with handling of the packages the smaller particles tended to separate from the bulk of the sample, enriching part of it, while depleting others.

We found that application of the iodine compounds as a solution resulted in a more even distribution of the iodine throughout the sample. Ferrous fumarate could not be applied as a solution, due to its low water solubility, and the iron rapidly segregated during normal handling of the sample containers, resulting in Fe concentrations that ranged between 25% and 175% of the initial 1000 ppm in different parts of the storage container.

Due to its low solubility, relatively dark colour, and tendency to turn to a darker colour with time, in our opinion ferrous fumarate is not a suitable carrier for iron in salt.

To overcome the distribution problem we started to use the complete sample for analysis. We subdivided it into two equal parts using a two-necked powder funnel, and repeated the procedure until the sample size was reduced to about 25g. We found that even after this extensive sample splitting the analyses were more reproducible if this subsample was first ground.

Table 5. Effect of sample grinding on measured iron content .

Sample	A41a		B21a		A42a	
	Unground	Ground	Unground	Ground	Unground	Ground
Average	7.143	8.218	8.652	8.377	2.804	3.891
Standard deviation Relative	1.82	1.20	2.71	0.12	0.47	0.16
Standard deviation %	25.56	14.62	31.39	1.53	16.87	4.11

Table 6. Effect of sample grinding on measured of iodine content

Sample	1	2	3	4	Average	Standard deviation	Relative standard deviation %
Unground	70.77	52.42	50.40	55.81	57.35	9.22	16.08
Ground	45.55	45.19	57.34	44.35	48.10	6.17	12.83

Colour

All of the samples prepared by the four kinds methods had a light pinkish brown tinge. In their freshly prepared form the colour of these samples would be marginally acceptable in our refined salt, and they would be routinely acceptable in unrefined salt, where some dark or rusty hues are regularly present. After storage the colour of the samples became darker, until they were brownish in color. These samples would be clearly unacceptable in refined salt, and may be only marginally acceptable in crude salt.

Due to its low solubility which makes its even distribution difficult, relatively dark colour, and tendency to turn to a darker colour with time, in our opinion ferrous fumarate is not a suitable carrier for iron in salt.

Flavour

There was a slight difference in taste between solutions of salt and double fortified salt. The difference in taste was minor, and we doubt that it would be objectionable, or even noticeable in a food matrix. Never-the-less this aspect of organoleptic acceptability must be considered when designing double-fortification systems.

Iron Stability

The iron content, of course remained constant, as neither the ferrous fumarate, nor its potential breakdown products are volatile.

For nutritional purposes the biologically available iron is the most important measure of the success of fortification. Since the iron must be in solution when it is absorbed in the body, the ratio of total iron to HCl soluble iron was determined, and used as an indicator of *in vitro* bioavailability. 1N HCl, similar to stomach acid was used. The amount of bioavailable iron remained essentially unchanged by any of the treatments. The results are summarized in Tables 7-10.

Due to its low solubility, relatively dark colour, and tendency to turn to a darker colour with time, in our opinion ferrous fumarate is not a suitable carrier for iron in salt.

Iodine stability

The critical problem with iodine addition is the potential for reducing or oxidizing the iodine in the salt to elemental iodine, or I_2. Elemental iodine readily sublimes, and although its vapour pressure at room temperature, or even at 40°C is low, if there is any air movement, the 40-60 mg/kg present in the sample would readily evaporate. In effect, we can assume that I_2 disappears from the salt as soon as it forms.

The results of the iodine determinations is presented in tables 11-14.

Table 7. Ratio of HCl Soluble Iron to Total Iron

Time months	KI Powder				
	0	1	2	3	6
1A	1.027	0.942	0.930	1.024	0.948
1B	1.027	1.111	0.913	0.965	1.057
1C	1.027	0.831	0.931	0.991	0.960
2A	1.027	0.902	0.991	1.109	1.034
2B	1.027	0.908	1.037	0.934	1.018
2C	1.027	1.104	0.996	0.927	1.057
3A	1.027	0.940	0.928	0.900	1.068
3B	1.027	1.022	1.028	1.050	0.998
3C	1.027	0.981	1.047	0.986	0.978
4A	1.027	0.952	0.915	1.003	0.957
4B	1.027	0.974	1.027	1.018	1.102
4C	1.027	0.933	0.971	0.993	1.021
	1.027	0.967	0.976	0.992	1.017

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars, 4; low-density polyethylene

A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized Soluble to Total Iron Ratio

Time months	KI Powder				
	0	1	2	3	6
1A	100.00	91.70	90.53	99.73	92.30
1B	100.00	108.15	88.85	93.92	102.92
1C	100.00	80.86	90.66	96.52	93.44
2A	100.00	87.82	96.48	107.96	100.71
2B	100.00	88.44	100.97	90.93	99.14
2C	100.00	107.51	96.96	90.24	102.91
3A	100.00	91.50	90.32	87.64	103.96
3B	100.00	99.54	100.11	102.27	97.13
3C	100.00	95.51	101.92	95.95	95.24
4A	100.00	92.70	89.05	97.65	93.18
4B	100.00	94.79	100.03	99.15	107.32
4C	100.00	90.87	94.56	96.65	99.38
	100.00	94.11	95.04	96.55	98.97

Table 8. Ratio of HCl Soluble Iron to Total Iron

Time	KI solution				
months	0	1	2	3	6
1A	0.990	1.023	0.988	0.973	1.022
1B	0.990	1.150	0.960	1.008	1.000
1C	0.990	0.907	0.948	0.963	1.022
2A	0.990	0.975	0.943	0.994	1.038
2B	0.990	1.058	1.044	0.978	1.061
2C	0.990	0.923	0.936	0.980	1.008
3A	0.990	1.050	1.043	1.020	1.028
3B	0.990	1.063	1.003	1.001	1.025
3C	0.990	0.920	0.992	0.996	1.084
4A	0.990	0.943	0.942	0.965	0.794
4B	0.990	1.048	1.008	0.928	1.060
4C	0.990	1.093	0.978	0.944	1.030
	0.990	1.013	0.982	0.979	1.014

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars,
4; low-density polyethylene
A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized Soluble to Total Iron Ratio

Time	KI solution				
months	0	1	2	3	6
1A	100.00	103.33	99.79	98.28	103.29
1B	100.00	116.23	96.99	101.89	101.04
1C	100.00	91.61	95.82	97.28	103.31
2A	100.00	98.50	95.28	100.48	104.86
2B	100.00	106.86	105.46	98.82	107.26
2C	100.00	93.22	94.53	99.06	101.88
3A	100.00	106.08	105.43	103.11	103.88
3B	100.00	107.46	101.33	101.13	103.54
3C	100.00	92.99	100.20	100.67	109.49
4A	100.00	95.33	95.20	97.55	80.24
4B	100.00	105.87	101.88	93.81	107.12
4C	100.00	110.48	98.82	95.40	104.09
	100.00	102.33	99.23	98.96	102.50

Table 9. Ratio of HCl Soluble Iron to Total Iron

Time	CaCO3 addition				
months	0	1	2	3	6
1A	1.032	0.833	0.978	1.009	1.079
1B	1.032	1.001	0.973	0.993	0.940
1C	1.032	0.905	0.971	1.000	0.943
2A	1.032	0.931	0.848	1.036	1.112
2B	1.032	0.980	0.934	1.025	1.060
2C	1.032	0.901	0.933	0.980	1.074
3A	1.032	0.957	1.028	0.973	0.968
3B	1.032	0.828	1.025	1.089	1.211
3C	1.032	1.080	0.895	0.979	1.039
4A	1.032	0.916	0.970	0.960	1.069
4B	1.032	1.024	0.836	0.993	0.992
4C	1.032	0.966	0.866	1.006	0.937
	1.032	0.943	0.938	1.004	1.035

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars,
4; low-density polyethylene
A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized Soluble to Total Iron Ratio

Time	CaCO3 addition				
months	0	1	2	3	6
1A	100.00	80.66	94.78	97.71	104.57
1B	100.00	97.00	94.28	96.21	91.02
1C	100.00	87.63	94.02	96.83	91.31
2A	100.00	90.18	82.16	100.37	107.70
2B	100.00	94.96	90.44	99.26	102.70
2C	100.00	87.24	90.34	94.93	103.99
3A	100.00	92.69	99.55	94.28	93.81
3B	100.00	80.19	99.32	105.52	117.33
3C	100.00	104.61	86.69	94.86	100.65
4A	100.00	88.75	93.97	93.03	103.52
4B	100.00	99.20	80.94	96.20	96.14
4C	100.00	93.59	83.91	97.44	90.74
	100.00	91.39	90.87	97.22	100.29

Table 10. Ratio of HCl Soluble Iron to Total Iron

Time	MgCl2 addition				
months	0	1	2	3	6
1A					
1B					
1C					
2A					
2B					
2C					
3A					
3B					
3C					
4A	1.007	0.971	0.932	0.986	0.971
4B	1.007	0.943	0.911	1.025	1.039
4C	1.007	0.914	1.009	0.937	0.959
	1.007	0.943	0.951	0.982	0.990

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars, 4; low-density polyethylene

A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized Soluble to Total Iron Ratio

Time	MgCl2 addition				
months	0	1	2	3	6
1A					
1B					
1C					
2A					
2B					
2C					
3A					
3B					
3C					
4A	100.00	96.43	92.56	97.88	96.45
4B	100.00	93.68	90.45	101.76	103.17
4C	100.00	90.79	100.19	93.00	95.27
	100.00	93.63	94.40	97.55	98.30

Table 11. Iodine content of salt

Treat-ment	Powder addition				
	0 month	1 month	2 months	3 months	6 months
1A	42.70	24.85	12.87	12.93	20.01
1B	56.37	18.14	12.29	20.04	13.80
1C	50.94	14.47	12.52	10.67	15.58
2A	60.81	21.02	13.91	17.61	14.23
2B	68.75	14.58	14.01	13.02	13.78
2C	45.96	18.54	12.20	23.09	18.61
3A	56.60	44.63	61.62	70.78	56.08
3B	55.51	12.93	12.79	15.01	15.24
3C	52.10	16.68	20.42	32.32	12.05
4A	65.60	39.55	13.28	15.65	17.53
4B	63.30	23.09	12.92	16.56	13.16
4C	73.84	23.91	9.47	9.78	12.00
Average	57.71	22.70	17.36	21.45	18.51

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars, 4; low-density polyethylene
A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized iodine content of salt

Treat-ment	Powder addition				
	0 month	1 month	2 months	3 months	6 months
1A	100.00	58.20	30.14	30.28	46.86
1B	100.00	32.18	21.80	35.55	24.48
1C	100.00	28.41	24.58	20.94	30.58
2A	100.00	34.57	22.87	28.96	23.40
2B	100.00	21.21	20.38	18.94	20.04
2C	100.00	40.34	26.54	50.23	40.50
3A	100.00	78.85	108.87	125.05	99.07
3B	100.00	23.29	23.04	27.04	27.46
3C	100.00	32.02	39.19	62.04	23.12
4A	100.00	60.29	20.24	23.86	26.73
4B	100.00	36.48	20.41	26.16	20.79
4C	100.00	32.38	12.83	13.24	16.26
Average	100.00	39.85	30.91	38.52	33.27

Table 12. Iodine content of salt

Treat-ment	KI solution				
	0 month	1 month	2 months	3 months	6 months
1A	55.73	25.41	17.45	26.94	18.84
1B	57.27	15.66	16.03	16.71	13.93
1C	59.59	11.81	18.02	18.37	18.30
2A	57.78	20.53	17.85	20.53	22.23
2B	59.10	13.20	18.57	19.05	20.08
2C	57.24	13.35	16.02	18.24	20.36
3A	57.40	42.21	42.93	32.98	31.30
3B	59.59	15.02	15.40	18.43	10.63
3C	57.53	13.95	13.72	16.97	13.50
4A	59.60	19.76	16.27	19.19	23.15
4B	56.77	13.37	16.09	20.81	14.33
4C	54.41	12.38	12.83	13.72	15.28
Average	57.67	18.05	18.43	20.16	18.49

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars, 4; low-density polyethylene

A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized iodine content of salt

Treat-ment	KI solution				
	0 month	1 month	2 months	3 months	6 months
1A	100.00	45.59	31.31	48.34	33.80
1B	100.00	27.34	27.99	29.18	24.33
1C	100.00	19.82	30.24	30.83	30.70
2A	100.00	35.53	30.89	35.53	38.47
2B	100.00	22.34	31.42	32.23	33.98
2C	100.00	23.32	27.99	31.87	35.56
3A	100.00	73.54	74.79	57.45	54.54
3B	100.00	25.21	25.84	30.94	17.84
3C	100.00	24.25	23.85	29.49	23.47
4A	100.00	33.15	27.30	32.19	38.85
4B	100.00	23.55	28.34	36.66	25.24
4C	100.00	22.75	23.58	25.22	28.07
Average	100.00	31.37	31.96	34.99	32.07

Table 13. Iodine content of salt

Treat-ment	CaCO3 addition				
	0 month	1 month	2 months	3 months	6 months
1A	55.06	37.25	14.85	12.98	11.66
1B	59.42	31.61	6.58	14.41	5.35
1C	61.07	39.87	7.63	8.41	7.49
2A	58.58	21.67	9.49	11.78	14.79
2B	59.45	33.20	11.19	17.84	9.45
2C	61.01	28.75	8.87	13.46	13.40
3A	59.53	48.61	17.17	14.80	13.75
3B	57.16	36.37	6.24	15.65	9.24
3C	62.08	33.11	6.89	10.54	9.80
4A	61.90	32.55	14.73	15.41	15.19
4B	57.35	28.48	9.37	14.75	8.28
4C	57.80	22.86	6.47	7.71	8.92
Average	59.20	32.86	9.96	13.14	10.61

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars, 4; low-density polyethylene

A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized iodine content of salt

Treat-ment	CaCO3 addition				
	0 month	1 month	2 months	3 months	6 months
1A	100.00	67.65	26.97	23.57	21.18
1B	100.00	53.20	11.07	24.25	9.00
1C	100.00	65.29	12.49	13.77	12.26
2A	100.00	36.99	16.20	20.10	25.25
2B	100.00	55.85	18.82	30.00	15.90
2C	100.00	47.12	14.54	22.06	21.96
3A	100.00	81.66	28.84	24.86	23.09
3B	100.00	63.63	10.92	27.38	16.16
3C	100.00	53.33	11.10	16.98	15.79
4A	100.00	52.58	23.80	24.90	24.53
4B	100.00	49.66	16.34	25.72	14.44
4C	100.00	39.55	11.19	13.34	15.43
Average	100.00	55.51	16.86	22.24	17.92

Table 14. Iodine content of salt

Treat-ment	MgCl2 addition				
	0 month	1 month	2 months	3 months	6 months
1A					
1B					
1C					
2A					
2B					
2C					
3A					
3B					
3C					
4A	64.28	6.67	6.23	3.05	4.05
4B	58.05	4.68	1.85	3.49	4.87
4C	54.26	3.46	2.45	2.79	2.41
Average	58.86	4.94	3.51	3.11	3.78

1: high-density polyethylene bags, 2; paper bags, 3; polypropylene jars, 4; low-density polyethylene
A: room conditions, B: 40°C.+100% RH, C: 40 °C + 60% RH, respectively.

Normalized iodine content of salt

Treat-ment	MgCl2 addition				
	0 month	1 month	2 months	3 months	6 months
1A					
1B					
1C					
2A					
2B					
2C					
3A					
3B					
3C					
4A	100.00	10.38	9.69	4.74	6.30
4B	100.00	8.06	3.18	6.00	8.39
4C	100.00	6.38	4.51	5.13	4.44
Average	100.00	8.39	5.79	5.29	6.38

The results indicate that most of the iodine loss occurs in the first month of storage. In case of KI addition either as powder, or as an aqueous solution approximately two thirds of the iodine applied to the sample disappeared in the first month, but the amount remaining after six months was similar to that at one month.

The addition of iodine prepared by co-drying a solution containing 4 g $CaCO_3$ per g KI did not seem to improve the uniformity or the stability of iodine. This is contrary to an earlier report in the scientific literature.

The effect of magnesium chloride addition was dramatic. As indicated earlier, this is a hygroscopic impurity normally found in crude, unrefined salt. It picked up moisture immediately, and its moisture content was some 10 times that of the other samples. Likely as a result of this moisture, the iodine oxidation reaction was greatly speeded up, and in a month more than 90 % of the iodine initially present on the salt has disappeared.

All of the analyses contain a fairly large variability. This is primarily due to the uneven distribution of iodine and iron in the salt samples, due to both the mixing process, which is difficult to do on a small scale, and the post-mixing segregation of the salt. The standard deviation of replicate analyses has been greatly improved during the program, as we adopted the multiple splitting of the whole sample, and we further ground the final few grams of sample obtained.

Effect of storage conditions

The results for iodine, listed in Tables 11-14 show that the high temperature / high humidity samples had the highest loss of iodine during storage for all storage materials. The exact extent of this difference varied with the type of treatment and storage material. The results confirmed the fact that the chemical breakdown and evaporation of iodine is accelerated by both moisture and elevated temperature. This result was fully expected.

The effect of storage medium was less marked. The difference between the four types of containers was not large enough to clearly identify differences in performance. While we expected the polypropylene jars to perform best and paper the worst, since the bags were not heat sealed there was sufficient air penetration and movement in all bags to prevent differentiation. Still, the most effective treatment was powder addition, stored at room temperature in a polypropylene jar, where after 6 months 99% of the original iodine remained. Unfortunately the variability in this sample was large, and one must be careful not to attribute too much significance to this result.

Since the salt will be stored in the final users' homes for a lengthy period during use, the salt will be essentially open to the atmosphere, independently of the type of bag used. Unfortunately the completely closable jars are probably not economically viable where fortification is needed. The field technology must be able to stand up to the rigors presented by the end user, although the sparing effect of a sealed system during distribution could be significant.

Conclusions and Recommendations

The results clearly indicated that iodine is rapidly lost after initial mixing, but the amount retained remains essentially constant after the first 1-2 months. In most treatments approximately a third of the iodine initially applied to the sample were retained. This leaves open the possibility of overdosing the salt initially with the aim of achieving a residual iodine level of ~40 mg/kg. It is not possible to determine from the results whether the rate of iodine depletion would remain proportional if the initial concentration was, say, tripled, or whether the concentration would continue to decline to 10-15 mg/kg residual iodine independently of the starting value. We suspect that this is most likely, but it can be readily determined experimentally.

Calcium chloride did not have a sparing effect on iodine, despite contrary indications in the literature. $CaCO_3$ is not soluble enough in cold water to effectively encapsulate iodine, and thus its effect was minimal.

The HCl soluble iron, which is representative of the amount of bioavailable iron, remained essentially unchanged by any of the treatments, as did the ratio of soluble iron to total iron.

We found that application of the iodine compounds as a solution resulted in a more even distribution of the iodine throughout the sample. Ferrous fumarate could not be applied as a solution, due to its low water solubility, and the iron rapidly segregated during normal handling of the sample containers, resulting in Fe concentrations that ranged between 25% and 175% of the initial 1000 ppm in different parts of the storage container. Due to its low solubility, relatively dark colour, and tendency to turn to a darker colour with time, ferrous fumarate is not a suitable carrier for iron in salt.

The effect of the packaging materials was overshadowed by the other variables. None of the packaging materials was clearly better than any other. This may have been due to the fact that the polymer bags were not heat sealed, and thus some moisture penetration was possible.

The highest iodine losses were observed at 40° C, 100% relative humidity. This is expected in systems where mass transfer is not highly restricted. We were hoping that the waterproof barrier materials would protect the salt, but this will not happen in an unsealed bag, and accordingly, it is unlikely to happen in the end-users' homes.

The most important finding of the study was the effect of magnesium chloride, a hygroscopic impurity often found in unpurified salt. It dramatically increased the moisture content of the salt, and resulted in the almost immediate loss of more than 90% of the added iodine.

The work demonstrated that it is important that adsorbed water, iron and iodine do not come into contact on the salt surface. The use of refined (purified)

salt is technically feasible, but it would be economically unviable. It is imperative, therefore, that the iron and iodine compounds be segregated. Better results could be achieved by encapsulating the iodine in a sparingly water soluble compound such as sodium hexametaphosphate or dextrin, which would prevent the oxidation or reduction of the iodine compounds until the salt system is solubilized during food preparation. It is preferable to encapsulate the iodine, since even at a 2% loading in the carrier, it would represent only 0.25% of the volume of the formulation. Segregation problems could be reduced by controlling particle size of the encapsulated iodine to a range similar to that of the salt particles.

There is no economic, or technical difficulty in preparing and applying a pre-formed iodine additive used at the 0.25% level, since the iron itself will be at the 0.1-0.2% level, depending on the compound selected.

Since 20+ more times as much iron is used as iodine, its encapsulation would result in a major component (5-10 %) n the final product.

or to prepare pre-mixes with high concentrations of iron and iodine separately, and use these to prepare the final formulation.

Despite of the losses of iodine experienced in this project, we are confident that a cost-effective, simple industrial process for double fortification is possible, but its development requires the systematic solution of the specific problems identified in this study. The proposed program of laboratory investigations attached in the appendix will demonstrate the feasibility of several approaches, forming the basis of an effective technological scale-up.

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APPENDIX

DOUBLE FORTIFICATION OF SALT

A proposal submitted to
The Micronutrient Initiative

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Background

Over the past decade the magnitude and consequences of global malnutrition have been increasingly recognized. Deficiencies in small quantities of micronutrients, especially iodine and iron, severely affect more than a third of the world's population. In the less developed countries these deficiencies have serious public health consequences, especially for women and young children.

The lack of iodine in the soil and water and thus, in food, leads to Iodine Deficiency Disorders (IDD) which includes goitre and a wide spectrum of mental and intellectual defects of varying degrees of severity including cretinism, paralysis and deaf-mutism. IDD can also lead to stunted growth and development, miscarriages, still births and infant deaths.

Anemia due to iron deficiency results in a major reduction in work capacity and impaired immune response which leads to a higher incidence of infection, increased risk of maternal and fetal morbidity, and reduction in body growth. The combined impact of these deficiencies results in a severe retardation of social and economic development of entire populations.

The fortification of commonly used foods is an important component of the strategy to combat micronutrient malnutrition. Salt is an ideal carrier of micronutrients in view of its almost universal coverage and uniform regional consumption. Iodized or iodated salt has long been available in developed countries and the problem of iodine deficiency has been virtually eliminated in North America and most European countries. Yet, because the severity and extent of IDD were not widely recognized until recently most of the affected countries begun to take steps towards universal iodization of salt only in the past few years. Many developing countries which now have iodization programs in place, have begun to achieve a significant reduction in IDD.

Encouraged by the progress made in several countries in implementing successful salt iodization programs, efforts have been directed to examining the feasibility of fortifying salt with iron along with iodine. With production and monitoring infrastructure for iodization programs already in place, such an integration and coordination would be the most cost efficient method of ensuring adequate levels of both iron and iodine in the population.

This poses a challenge in developing a formulation in which both the iodine and iron are stable and bioavailable. When attempts were initially made in the mid 1980's to incorporate iodine and iron in salt at the same time, there were problems with the stability of both micronutrients.

Salt can be iodized with either potassium iodide (KI) or iodate (KIO_3). While the former is stable in refined dry salt, the latter shows better stability in low-quality salt in poor packaging. Ferrous iron is stable in an acid

medium, whereas the iodine salts are slightly alkaline in solution. In an alkaline medium ferrous iron can oxidize to ferric, which is not as soluble, and therefore the bioavailability of iron is lowered.

When the iron is added as ferrous sulphate to an impure salt, which is hygroscopic, the system becomes acidic. In an acid medium the oxidation of the iodide to iodine takes place producing free iodine, which vaporizes, and is lost. Potassium iodate is an oxidizing agent. When it is mixed with ferrous iron it tends to oxidize Fe^{++} to Fe^{+++}, while it is reduced to the volatile I_2 or KI. In order to tackle the problem of incompatibility between iron and iodine salts, two approaches have been proposed: using ferrous sulphate with a chelating polyphosphate stabilizer along with potassium iodide (Rao, N.B.S. 1990); and using ferrous fumarate along with potassium iodide (Venkatesh Mannar et al. 1989). In India both approaches have been tested and workable formulations have been proposed:

i. Narasinga Rao of the National Institute of Nutrition developed a formula using ferrous sulphate (1000 ppm Fe), potassium iodide (20 ppm I_2) and a stabilizer (a chelating polyphosphate). He has reported that the bioavailability and stability of the double fortified salt under different conditions of storage and acceptability were found to be good. The formulation proposed by Rao is:

Ferrous sulphate ($FeSO_4.7H_2O$)	5000 ppm	(1000 ppm Fe)
Potassium iodide	40 ppm	(30 ppm I_2)
Stabilizer (phosphate)	1 %	

However; the analysis of salt from a larger-scale test showed less than 3% of the initial iodine levels after distribution.

ii. After tests with various iron and iodine compounds, Venkatesh Mannar et al. (1989) reported that ferrous fumarate and potassium iodide represent a workable combination without stabilizers. Ferrous fumarate, which is a poorly soluble, but biologically well absorbed iron compound, has a pH close to 7 in solution, and it should be stable to oxidation. While it is naturally reddish brown in colour, at the small concentration of 3 g/kg salt (~1000 ppm Fe) it imparts only a light pink-brown colour to the salt, and did not seem to deteriorate with time. At this concentration it is less likely than $FeSO_4.7H_2O$ to cause organoleptic problems. Owing to the fine particle size of ferrous fumarate in its usual commercial form (200 mesh), it can be added in a dry form as a rich premix and still get it evenly dispersed in the salt. Its toxicity is less than that of ferrous sulphate, and its effect on the stomach lining is less irritating than that of ferrous sulphate or ferrous gluconate. Potassium iodide, unlike potassium iodate is not an oxidizing agent, and therefore it will not react with ferrous fumarate. Salt fortified with ferrous fumarate and potassium iodide is of a very light brownish colour and does not deteriorate with time, provided that

it is kept sealed in waterproof packing. They proposed the following formulation for double fortification of salt:

Ferrous fumarate	3050 ppm	(1000 ppm Fe)
Potassium iodide	65 ppm	(50 ppm I_2)

The test report indicated that iron and iodine levels in the double-fortified salt were not depleted in 8 weeks of storage after preparation.

Both reports of successful double-fortification trials used potassium iodide as a source of iodine. This is a departure from conventional practice, since potassium iodate is currently used in most developing countries. KIO_3 is more stable than KI due, perhaps, to a lower water solubility, which is a problem in humid environments in which impure salt absorbs moisture in non-water-tight containers.

These reports seem to indicate that the use of potassium iodide in double fortification of salt will require that:

1. The salt should be refined to a well defined minimum purity level and dried before fortification in order to preserve the iodine and iron in the salt with minimal loss due to oxidation or hydrolysis.

2. The salt must be packed immediately after fortification in waterproof packaging.

If these approaches indeed work, the chemical advantages and the lower cost of KI will justify the extra processing.

In their most recent work Rao et al. will report on a system where sodium hexametaphosphate is used to stabilize the system.

Despite these encouraging reports, the technical feasibility of double-fortification of salt has not been unequivocally demonstrated, and the technology of large scale application has not yet been developed or tested.

Based on the previously reported work we have undertaken a 14 month program to test the effects of application and packaging technology on the long-term stability of double-fortified salt prepared by the technique of Manar et al.

There are two basic techniques for applying the fortifying agents to salt. The iodine and iron compounds can be dissolved in water, sprayed on the salt, and then dried. This assures a uniform coating of the salt particles with the fortifying agents, and ensures that they cannot separate from the salt during subsequent handling. The disadvantage of this technique is that the salt has to be dried after the blending step. In case of double-fortification there is an additional problem of chemical reaction between the iron and

iodine compounds in the solution, which may reduce the bioavailability and stability of both.

The other widely practiced technique involves the blending of finely powdered solids with the salt. This technique is simpler and cheaper, however great care must be taken to ensure that the solids are uniformly mixed, and that the fortifying agents do not segregate from the salt during transit and handling.

While we tested both of these approaches, to reduce the chance of reactions between the iron and iodine compounds we are also testing a third approach based on previously reported findings of Rao: the KI was slurried with $CaCO_3$ which acts as a stabilizing agent, and co-dried. This blend, and the ferrous compound can be then added as solids in a blender.

Each of these preparation techniques is being tested in four typical packaging materials under three conditions over the period of one year to ensure that both the iron and the iodine are retained in a bioavailable form.

Our preliminary results clearly show that a hygroscopic impurity in the salt will lead to a very rapid loss in iodine content. Despite the presence of calcium carbonate, ferrous fumarate gives a pinkish brown tinge to salt, which turns darker with time, indicating the oxidation of iron to its ferric form.

We believe that there is a need to look at other combinations of iron and iodine compounds, alone, and in the presence of stabilizing agents. We also feel that encapsulation of iodine, iron or both will result in a physical barrier between iron, iodine and oxygen, thus reducing the chance of undesirable interactions. While it would be desirable to develop and test the technology of double fortification of salt and to transfer this technology to the user sector as soon as possible, as the continued shortage of these micronutrients continues to take a grim toll of poor health and disabling child development, it is clear that a suitable technique for preparing a stable double-fortified salt is still not proven even on a laboratory scale. To achieve the goal of developing and deploying a viable technology for double fortification, a complete program of laboratory development, engineering scale-up and extensive laboratory and field-testing is required. Following the initial proof of the technical feasibility of double-fortification in the laboratory, the program must eventually include the following stages, some of which can run concurrently:

1. Nutritional testing of the selected formulations (2-4 months)

2. In vivo and in vitro bioavailability studies (2-4 months)

3. Pilot testing of the proposed processes (2-3 months)

4. Design of human nutritional trials for the best 1-2 treatments (1-2 months)

5. Field trials for the best 1-2 treatments (12 months ?)

6. Finalization of fortification techniques in pilot plant (1-2 months)

7. Engineering evaluation and design (3-4 months)

8. Technology transfer

The present proposal deals only with the laboratory scale development of one or more double-fortification techniques, in an effort to clearly demonstrate the technical feasibility of this technique, and narrowing the choice of technologies for further development.

Objectives

To achieve the ultimate goal of developing an industrially and economically viable process for the large-scale double fortification of salt, the proposed experimental program will determine the feasibility of this approach, by identifying the fortifying agents and techniques that result in a stable double-fortified salt under conditions of temperature, humidity and salt purity typically found in the proposed receptor countries.

The proposed program will evaluate the stability and in-vitro availability of iron and iodine in a number of double-fortified salt samples, prepared using a series of techniques: dry mixing, wet mixing, encapsulation and chemical stabilization.

Proposed Program

Background

Under an existing contract we are testing the storage stability of double fortified salt in a series of packaging systems, under a variety of storage conditions:

Ferrous fumarate	3050 ppm	(1000 ppm Fe)
Potassium iodide	65 ppm	(50 ppm I_2)

The test report indicated that iron and iodine levels in the double-fortified salt were not depleted in 8 weeks of storage after preparation.

1. 1 kg samples of salt were fortified to contain 50 mg/kg iodine and 1,000 mg/kg iron using potassium iodide and ferrous fumarate respectively. The reagents were added to the salt as a very finely divided powder, and blended to ensure uniformity.

2. The second series of samples was prepared by mixing salt with an aqueous solution of KI and ferrous fumarate in a V blender. The mixture was dried, sampled and bagged as in 1 above.

3. In an attempt to prevent the interaction of iron and iodine, $CaCO_3$, which is often used as a stabilizing agent for KI, was added as a powder containing 4 g $CaCO_3$ per g KI. This mixture was blended with salt and ferrous fumarate.

4. KI was spray dried from a solution of calcium chloride, thus micro-encapsulating it, to prevent its contact with the iron ions.

5. To simulate the effect of typical hygroscopic impurities of sea salt, the first run was repeated, using salt containing 1% magnesium chloride.

Six samples of each of the above preparations was packaged in 500g portions as follows:

1. High-density polyethylene bags
2. Paper bags
3. PVC containers
4 Low-density polyethylene bags

The packages are being stored under three conditions: ambient room temperature and humidity (~ 22 ° C, 50-70% RH), at elevated temperature and humidity (~ 40° C, 100% RH) and at elevated temperature and low humidity (~ 40° C, ~ 60 % RH).

Initial results have shown that the presence of magnesium chloride results in rapid absorption of water, which in turn, leads to the reaction of KI with iron, resulting in the loss of iodine. This can take place almost instantaneously in some cases. This indicates, that the iodine must be protected from contact with iron. Stabilizers, or microencapsulation seem to be the best route to achieving iodine stability.

Unfortunately, after storage ferrous fumarate imparts a noticeable reddish brown colouration to the salt, and its aqueous solution at concentrations found during food preparation (1-2%). This will be probably a serious impediment to its acceptance by even informed consumers.

Based on these preliminary results it seems prudent to explore a range of iron compounds and stabilization techniques, before field trials are planned.

Experimental Techniques:

Early results of our current test series have shown that there are many potentially viable approaches to the application of iodine and iron to salt. Unfortunately, there are also many pitfalls, where iodine is quickly lost even during the mixing process. We propose to investigate 40 different combinations of iron and iodine compounds, and application techniques.

The following iron compounds will be tested:

ferrous lactate
ferrous ammonium citrate
ferrous sulphate
Na Fe EDTA
modified ferric orthophosphate (Nobel, Sweden)

The iodine will be added in the form of potassium iodide and iodate. As stabilizers calcium carbonate, sodium hexametaphosphate and dextrose will be tested. We will test sodium hexametaphosphate, sodium chloride, dextrin, mono and diglycerides and dextrose as encapsulating agents.

The salt samples will be prepared by two-stage blending, and then stored in the best and worst packaging found thus far, under high temperature and humidity. The samples will be analyzed after preparation and after 1 and 3 months. Both pure salt and salt containing 1% $MgCl_2$ will be tested. This should give an indication of the relative cost and the feasibility of salt purification, compared with the cost of encapsulation or other treatment of the fortifying additives

For each sample the following analyses will be performed:

1. Moisture
2. Iron: - Fe, and soluble Fe, by atomic absorption
3. Iodine by neutron activation analysis

Bioavailability of iron and iodine will be estimated *in vitro* on the basis of solubility under physical; and chemical conditions found in the stomach: i.e. ~37°C, ~ 1N HCl with he optional use of digestive enzymes.

The colour and cost of the formulations will be evaluated.

The effect of double fortification on the taste and appearance of salt and on typical staple food items prepared with double fortified salt will be noted.

The most stable and economically potentially viable treatments will be stored for a further 3 months, and the analytical tests will be repeated, giving a reliable indication of long term stability.

We foresee that 2-4 acceptable approaches may emerge from this initial phase of the program. It is hoped that these will lead, eventually, to a development program, as outlined in the background.

An interim technical report will be submitted within a month of the half-way point of the program, i.e. within seven months of signing of the contract. At the end of the proposed program a final report will be submitted,

and it is our intention to publish the results in the scientific literature, after safeguarding any patentable inventions stemming from this work.

Intellectual Property

Both the University and the Micronutrient Initiative is interested in the rapid, unimpeded dissemination of any double-fortification technology developed through the proposed program. To control the use of these technologies, the University will obtain U.S. or Canadian patents on these developments, and grant a royalty-free, world-wide license to the Micronutrient Initiative. The cost of obtaining and maintaining the patent(s) will be borne by the Micronutrient Initiative, and is not included in the proposed budget. The decision to patent any invention will be made after consultation between the University and the Micronutrient Initiative.

Estimated Costs

The project will be carried out over a period of twelve months. The following budget breakdown is proposed:

Materials and supplies	$ 5,500
Equipment purchase and upgrading (One large oven, parts for spray dryer)	$ 3,500
Publication costs	$ 2,000
Labour	
K. Ramcharan, graduate student	$15,000
Subcontracts:	
J.Alberti, chemist @ $ 50,000 for 6 months	$ 25,000
L.L.Diosady 1 month @ $ 10,000, while on sabbatical leave	$ 10,000
GST on subcontracts	$ 2,450
Overhead at 13%	$ 8,248.50
Total	**$ 69,698.50**

Principal Investigators

The project will be carried out and coordinated by the food engineering group in the Department of Chemical Engineering and Applied Chemistry, under the direction of Professor L. L. Diosady. The program was

designed in cooperation with Mr. M. G. Venkatesh Mannar, who will be advising the University of Toronto group on all aspects of the project from his new position at the Micronutrients Initiative. Mr. Venkatesh Mannar is a chemical engineer with more than 20 years experience in salt production, refining and fortification. He has been associated with programs for the fortification of salt with iodine or iron in several countries. Professor Diosady is professor of food engineering with extensive industrial and academic experience in all aspects of food processing, development and analysis.

His brief curriculum vitae is appended.

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LEVENTE L. DIOSADY

Professional Profile

Levente L. Diosady is an Honour Graduate (1966) in Chemical Engineering from the University of Toronto. He is a registered Professional Engineer, and a designated Consulting Engineer in the Province of Ontario. After graduation he returned to the University of Toronto, where he obtained his M.A.Sc. (68) and Ph.D. (71) degrees in the Department of Chemical Engineering and Applied Chemistry.

In 1972 Dr. Diosady joined the Cambrian Engineering Group as a process engineer, and in 1974 he was appointed Director, Research and Development for the company. In this capacity he was responsible for establishing the company's research and contract analytical laboratories. He initiated an ambitious program of process development in the areas of edible oil processing and environmental control. Under his direction the laboratory group had grown to some 35 scientists and technicians by 1979, and performed some 10,000 contract analyses monthly for the food, feed and environmental control industries.

In October 1979 Dr. Diosady joined the University of Toronto, Department of Chemical Engineering and Applied Chemistry as Associate Professor, where he joined Dr. L.J.Rubin in establishing the first Canadian engineering program in food process engineering. Together they developed four undergraduate and three graduate courses, and initiated a multi-faceted research and development program. Dr. Diosady was promoted to Professor in 1985. In 1990 he has been appointed Adjunct Professor in the University of Guelph, School of Engineering.

Professor Diosady's research interests include vegetable oil processing, edible-oil refining and hydrogenation, extrusion, protein extraction by membrane processes, trace components of food and meat curing. He was the author of over 70 publications in refereed journals, and presented the results of the group's research in some 60 international scientific meetings in Canada and abroad.

The research has resulted in a total of 6 groups of patents, including those granted for the development of a nitrite-free meat curing system, and for a novel approach to canola processing. The Innovations Foundation of the University of Toronto received a Canada Award for Business Excellence in the Invention category in 1987 for the rapeseed extraction process developed by Professors Diosady and Rubin. A recently completed project developed a new process for chlorophyll removal from canola oil. It is now installed in a very large edible-oil refinery.

In addition to his academic activities, Dr. Diosady continues to consult in the areas of food processing, trace organic analysis, laboratory planning and R & D management. He is the President of Food BioTek

Corporation and he is a Director of Chemical Engineering Research Consultants Limited . He is Vice-Chairman of the Board of SGS Certification Services Inc.

Dr. Diosady is the Past-Chairman of the Expert Subcommittee on Energy, Canada Committee on Food and a member of the Expert Committee on Food Engineering. He is the past president of the Canadian Section of the American Oil Chemists' Society, the Food Engineering Section, Canadian Institute of Food Science and Technology. He was elected a Fellow of the Chemical Institute of Canada, Canadian Society of Chemical Engineering

Dr. Diosady is active in the cultural activities of the Hungarian-Canadian community: he is a founding director and Secretary Treasurer of the Hungarian Research Institute of Canada, a research ancillary of the University of Toronto; a founding director and vice-president of the Rákóczi Foundation, and past president of the Hungarian-Canadian Engineers' Association.